WHAT IS CLAIMED IS:

1. A bi-specific chimeric antigen receptor (CAR) that binds to CD19 and CD20, the CAR comprising:

(a) an extracellular domain that comprises (i) a first antigen-binding domain that binds to CD19 and (ii) a second antigen-binding domain that binds to CD20;

(b) a transmembrane domain comprising a first CD28 polypeptide; and

(c) an intracellular domain comprising a modified CD3ζ polypeptide that comprises a native ITAM1, an ITAM2 variant, and an ITAM3 variant, wherein each of the ITAM2 variant and the ITAM3 variant comprises two loss-of-function mutations.

2. The CAR of claim 1, wherein the first anti-CD19 antigen-binding domain comprises:

(a) a first heavy chain variable region (V_H) and a first light chain variable region (V_L), wherein the first V_H comprises a V_H CDR1, a V_H CDR2, and a V_H CDR3 of a V_H comprising the amino acid sequence set forth in SEQ ID NO: 15, and/or the first V_L comprises a V_L CDR1, a V_L CDR2, and a V_L CDR3 of a V_L comprising the amino acid sequence set forth in SEQ ID NO: 16, and wherein optionally the V_H CDR1, V_H CDR2, V_H CDR3, V_L CDR1, V_L CDR2, and V_L CDR3 are identified according to the Kabat numbering system, the Chothia numbering system, the AbM numbering system, the Contact numbering system, or the IMGT Information System®;

(b) a first V_H and a first V_L, and wherein the first V_H comprises a V_H CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 9 or a conservative modification thereof, a V_H CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 10 or a conservative modification thereof, and a V_H CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 11 or a conservative modification thereof; and/or the first V_L comprises a V_L CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 12 or a conservative modification thereof, a V_L CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 13 or a conservative modification thereof, and a V_L CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 14 or a conservative modification thereof;

(c) a first V_H and a first V_L, and wherein the first V_H comprises a V_H CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 9, a V_H CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 10, and a V_H CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 11; and/or the first V_L comprises a V_L CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 12, a V_L CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 13, and a V_L CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 14;

(d) a first V_H and a first V_L, and wherein the first V_H comprises an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% identical or homologous to the amino acid sequence set forth in SEQ ID NO: 15; and/or the first V_L comprises an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% identical or homologous to the amino acid sequence set forth in SEQ ID NO: 16; or

(e) a first V_H and a first V_L, and wherein the first V_H comprises the amino acid sequence set forth in SEQ ID NO: 15; and/or the first V_L comprises the amino acid sequence set forth in SEQ ID NO: 16.

3. The CAR of claim 1 or 2, wherein the second anti-CD20 antigen-binding domain comprises:

(a) a second V_H and a second V_L, wherein the second V_H comprises a V_H CDR1, a V_H CDR2, and a V_H CDR3 of a V_H comprising the amino acid sequence set forth in SEQ ID NO: 27, and/or the second V_L comprises a V_L CDR1, a V_L CDR2, and a V_L CDR3 of a V_L comprising the amino acid sequence set forth in SEQ ID NO: 28, and wherein optionally the V_H CDR1, V_H CDR2, V_H CDR3, V_L CDR1, V_L CDR2, and V_L CDR3 are identified according to the Kabat numbering system, the Chothia numbering system, the AbM numbering system, the Contact numbering system, or the IMGT Information System®;

(b) a second V_H and a second V_L, wherein the second V_H comprises a V_H CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 21 or a conservative modification thereof, a V_H CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 22 or a conservative modification thereof, and a V_H CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 23 or a conservative modification thereof; and/or the second V_L comprises a V_L CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 24 or a conservative modification thereof, a V_L CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 25 or a conservative modification thereof, and a V_L CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 26 or a conservative modification thereof;

(c) a second V_H and a second V_L, wherein the second V_H comprises a V_H CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 21, a V_H CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 22, and a V_H CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 23; and/or the second V_L comprises a V_L CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 24, a V_L CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 25, and a V_L CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 26;

(d) a second V_H and a second V_L, wherein the second V_H comprises an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% identical or homologous to the amino acid sequence set forth in SEQ ID NO: 27; and/or the second V_L comprises an amino acid sequence that is at least about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% identical or homologous to the amino acid sequence set forth in SEQ ID NO: 28; or

(e) a second V_H and a second V_L, and wherein the second V_H comprises the amino acid sequence set forth in SEQ ID NO: 27; and/or the second V_L comprises the amino acid sequence set forth in SEQ ID NO: 28.

4. The CAR of claim 3, wherein:

(a) the first anti-CD19 antigen-binding domain comprises a first linker between the first V_H and the first V_L, wherein optionally the first linker comprises the amino acid sequence set forth in SEQ ID NO: 1; and/or wherein optionally the first V_H and the first V_L are positioned from the N- to the C-terminus: V_L-V_H; and/or

(b) the second anti-CD20 antigen-binding domain comprises a second linker between the second V_H and the second V_L, wherein optionally the second linker comprises the amino acid sequence set forth in SEQ ID NO: 2, and/or wherein optionally the second V_H and the second V_L are positioned from the N- to the C-terminus: V_H-V_L.

5. The CAR of any one of claims 1-4, wherein:

(a) the first anti-CD19 antigen-binding domain comprises a first anti-CD19 single-chain variable fragment (scFv) that binds to CD19, wherein optionally the first anti-CD19 scFv comprises the amino acid sequence set forth in SEQ ID NO: 17; and/or

(b) the second anti-CD20 antigen-binding domain comprises a second anti-CD20 single-chain variable fragment (scFv) that binds to CD20, wherein optionally the second anti-CD20 scFv comprises the amino acid sequence set forth in SEQ ID NO: 29.

6. The CAR of any one of claims 1-5, further comprising:

(a) a third linker between the first anti-CD19 antigen-binding domain and the second anti-CD20 antigen-binding domain, wherein optionally the third linker comprises the amino acid sequence set forth in SEQ ID NO: 3; and/or

(b) a hinge region, wherein optionally the hinge region comprises a second CD28 polypeptide, and optionally the second CD28 polypeptide comprises amino acids 114 to 152 of SEQ ID NO: 35.

7. The CAR of any one of claims 1-6, wherein:

(a) the first anti-CD19 antigen-binding domain is positioned downstream of the second anti-CD20 antigen-binding domain;

(b) a leader is covalently joined to the N-terminus of the second anti-CD20 antigen-binding domain, wherein optionally the leader comprises a CD8 polypeptide, and optionally the CD8 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 33; and/or

(c) the first CD28 polypeptide is a transmembrane domain sequence of CD28, wherein optionally the first CD28 polypeptide comprises amino acids 153 to 179 of SEQ ID NO: 35

8. The CAR of any one of claims 1-7, wherein:

(a) each of the two loss-of-function mutations is at a tyrosine amino acid residue;

(b) the ITAM2 variant comprises the amino acid sequence set forth in SEQ ID NO: 45;

(c) the ITAM3 variant comprises the amino acid sequence set forth in SEQ ID NO: 49;

(d) the native ITAM1 comprises the amino acid sequence set forth in SEQ ID NO: 39;

(e) the modified CD3ζ polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 51; and/or

(f) the intracellular signaling domain further comprises a co-stimulatory signaling region, and wherein optionally the co-stimulatory signaling region comprises a third CD28 polypeptide, and optionally the third CD28 polypeptide is a signaling domain sequence of CD28, which optionally comprises amino acids 180 to 220 of SEQ ID NO: 35.

9. The CAR of any one of claims 1-8, comprising the amino acid sequences set forth in SEQ ID NO: 54.

10. A nucleic acid encoding the CAR of any one of claims 1-9, wherein optionally nucleic acid comprises the nucleotide sequence set forth in SEQ ID NO: 55.

11. A vector comprising the nucleic acid of claim 10, wherein optionally the vector is a viral vector, which is optionally a retroviral vector.

12. A cell comprising the CAR of any one of claims 1-9, the nucleic acid of claim 10, or the vector of claim 11, wherein optionally:

(a) the CAR is constitutively expressed on the surface of the cell;

(b) the cell is an immunoresponsive cell or an immune effector cell; and/or

(c) (1) the cell is a cell of the lymphoid lineage or a cell of the myeloid lineage, and optionally (i) the cell of lymphoid lineage is selected from the group consisting of T cells, Natural Killer (NK) cells, B cells, and stem cells from which lymphoid cells may be differentiated; or (ii) the cell of the myeloid lineage is selected from the group consisting of monocytes, macrophages, neutrophils, dendritic cells, basophils, neutrophils, eosinophils, megakaryocytes, mast cell, erythrocyte, thrombocytes, and stem cells from which myeloid cells may be differentiated; or

(2) the cell is selected from the group consisting of a T cell, a B cell, a Natural Killer (NK) cell, a macrophage, an innate lymphoid cell (ILC), a cytokine induced killer (CIK) cell, a lymphokine activated killer (LAK) cell, a stem cell from which a lymphoid cell may be differentiated, a stem cell from which a myeloid cell may be differentiated, and combinations of the foregoing; or

(3) the cell is a T cell, and optionally the T cell is selected from the group consisting of helper T cells, cytotoxic T cells (CTLs), memory T cells, regulatory T cells, tumor-infiltrating lymphocyte (TIL), Natural Killer T cells, mucosal associated invariant T cells, αβ T cells, and γδ T cells.

13. A composition comprising the cell of claim 12, wherein optionally:

(a) the composition is a pharmaceutical composition further comprising: a pharmaceutically acceptable carrier; and/or

(b) the composition comprises between about 1×10^6 and about 5×10^8 of the cells

14. Use of the cell of claim 12, or the composition of claim 13 for use in the manufacture of a medicament for inhibiting growth of a target cell expressing at least one B-lymphocyte antigen, wherein optionally:

(a) the target cell is autologous or allogenic;

(b) the target cell is a tumor cell; and/or

(c) the at least one B-lymphocyte antigen is selected from the group consisting of CD19, CD20, and a combination thereof, and optionally:

(i) the target cell expresses a detectable level of CD19 and a detectable level of CD20;

(ii) the target cell expresses a detectable level of CD20 and a low or non-detectable level of CD19; or

(iii) the target cell expresses a detectable level of CD19 and a low or non-detectable level of CD20.

15. Use of the cell of claim 12, or the composition of claim 13 for the manufacture of a medicament for treating a B-lymphocyte antigen-associated disease in a subject, treating a hematologic cancer in a subject, or treating an autoimmune disease in a subject, wherein optionally the subject is a human subject, and wherein optionally:

(a) the B-lymphocyte antigen is selected from the group consisting of CD19, CD20, and a combination thereof and/or the B-lymphocyte antigen-associated disease is a cancer or an autoimmune disease;

(b) the hematologic cancer is selected from the group consisting of acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), B cell leukemia, multiple myeloma, Hodgkin's lymphoma, non-Hodgkin's lymphoma (NHL), diffuse large B cell lymphoma (DLBCL), Burkitt lymphoma, mantle cell lymphoma (MCL), and follicular lymphoma (FL);

(c) the autoimmune disease is selected from the group consisting of multiple sclerosis, systemic lupus erythematosus (SLE), Sjogren's, AL amyloidosis, Sjogren's, AL amyloidosis, IgG4-related disease (IgG4-RD), inflammatory myopathies (e.g., myositis), scleroderma, pemphigus vulgaris, chronic inflammatory demyelinating polyneuropathy (CIDP), Guillain-Barré syndrome (GBS), stiff-person's syndrome, rheumatoid arthritis, neuromyelitis optica spectrum disorder (NMOSD), myasthenia

gravis, N-methyl-D-aspartate receptor (NMDAR) encephalitis, anti-myelin oligodendrocyte glycoprotein (MOG) syndrome, myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), membranous nephropathy (MN), IgA nephropathy (IgAN), Type 1 diabetes, anti-neutrophil cytoplasmic antibody (ANCA) vasculitis, thrombocytopenia purpura, hemolytic anemia (AIHA), multifocal motor neuropathy (MMN), inflammatory bowel disease (IBD), celiac disease, Crohn's disease, ulcerative colitis, and ankylosing spondylosis;

(d) the cell or composition exhibits cytotoxic and/or cytolytic activity against a target cell in the subject, wherein the target cell expresses i) a detectable level of CD19 and a detectable level of CD20; ii) a detectable level of CD20 and a low or non-detectable level of CD19; iii) a detectable level of CD19 and a low or non-detectable level of CD20, and optionally the cytotoxic and/or cytolytic activity is dose-dependent and/or long-term;

(e) the cell or composition does not induce graft-versus-host disease;

(f) the cell or composition induces no or minimal alloreactivity against a HLA-mismatched cell positive for CD19 and/or CD20 in the subject; and/or

(g) the cell or composition exhibit no or minimal cytotoxic and/or cytolytic activity against an off-target cell in the subject, wherein the off-target cell is negative for CD19 and CD20.

16. A method for producing the cell of claim 12, the method comprising: introducing into a cell the CAR of any one of claims 1-9, the nucleic acid of claim 10, or the vector of claim 11.